Section 006: 510(k) Summary

510(k) Summary – ADVIA Centaur VB12 Master Curve Material

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

The assigned 510(k) Number: k140505

1. Applicant Information	
Mailing Address:	Siemens Healthcare Diagnostics Inc. 511 Benedict Avenue Tarrytown, NY 10591 USA
Contact Person:	Fatima Pacheco Regulatory Clinical Affairs Specialist
Phone Number:	(914) 524-2450
Fax Number:	(914) 524-3579
E-mail Address:	fatima.pacheco@siemens.com
Date Prepared:	February 24, 2014
2. Device Name	**ADVIA Centaur® Vitamin B12 (VB12) Master Curve Material**
Proprietary Name:	Quality Control materials for ADVIA Centaur VB12 assay
Measurand:	Master Curve Material (MCM) for ADVIA Centaur VB12 assay
Type of Test:	21 CFR 862.1660, Quality Control Material
Regulation Section:	Class I Reserved
Classification:	JJX – Single (Specified) Analyte Controls (Assayed and
Products Code:	Unassayed)
Panel:	Clinical Chemistry (75)
3. Predicate Device Name	Elecsys Vitamin B12 CalCheck
Predicate 510(k) No:	K060755
4. Device Description:	ADVIA Centaur® Vitamin B12 Master Curve Material is an *in vitro* diagnostic product containing various levels of vitamin B_{12} in buffered human serum albumin with sodium azide (0.2%) and preservatives. Each set contains six levels (MCM1–6); with a fill volume of 1.0 mL per level. VB12 MCMs are ready-to-use liquid products. MCM1contains no analyte. The MCMs assigned values are lot-specific of target values: 0.00, 100,250, 500, 1000, and 2200 pg/mL.

CAUTION! POTENTIAL BIOHAZARD: Contains human source material. While each human serum or plasma donor unit used in the manufacture of this product was tested by FDA-approved methods and found nonreactive for hepatitis B surface antigen (HBsAg), antibody to hepatitis C (HCV), and antibody to HIV-1/2, all products manufactured using human source material should be handled as potentially infectious. Because no test method can offer complete assurance that hepatitis B or C viruses, HIV, or other infectious agents are absent, these products should be handled according to established good laboratory practices.

5. **Intended Use:**

Indication for Use: See Indications for Use Statement below:
The ADVIA Centaur® Vitamin B12 (VB12) Master Curve Material is for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur VB12 assay.

Special Conditions for Use Statement(s): For prescription use only

Special Instrument Requirements: ADVIA Centaur® Systems
A description of the ADVIA Centaur system is documented in K971418. Subsequent modifications to the instrument have been reviewed and cleared in K032525 and K041133.

6. **Technological Characteristics and Substantial Equivalence Comparison with Predicate:** A comparison of the device features, intended use, and other information demonstrates that the ADVIA Centaur VB12 MCM is substantially equivalent to the predicate device as summarized in **Table 1**.

Table 1: Substantial Equivalence Comparison

SIMILARITIES		
	Candidate Device	**Predicate Device**
Item	ADVIA Centaur VB12 MCM	Elecsys Vitamin B_{12} CalCheck
Intended Use	The ADVIA Centaur Vitamin B12 (VB12) Master Curve Material is for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur VB12 assay.	For use in the verification of the calibration established by the Elecsys Vitamin B_{12} reagent on the indicated Elecsys and cobas e immunoassay analyzers.
Analyte	Vitamin B_{12}	Same
Use	Multiple Use	Same
Storage	2–8°C	Same
DIFFERENCES		
Form	Liquid	Lyophilized
Matrix	Human Serum Albumin	Human Serum
Levels	6	3
Stability	**Unopened** – Stable when stored unopened at 2–8°C until the expiration date on the vial label. **Opened** – Stable on-board for 4 hours.	**Unopened** – Stable at 2–8°C up to the expiration date printed on the bottle labels. **Reconstituted** – Stable for 4 hours at 20–25°C.

7. **Standard/Guidance Document References**

The following recognized standard and guidance documents were used:

- CEN 13640 Stability Testing of In Vitro Diagnostic Reagents
- Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators
- Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material

8. Test Principle

The MCMs are specifically intended for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur assays for use on the ADVIA Centaur systems. Customers may use MCMs for bi-annual calibration verification checks of the assay range and linearity in order to meet the requirements of hospital accreditation bodies.

9. Performance Characteristics

9.1 Analytical performance:

The following studies are not applicable for the purpose of this submission:

- *Precision/Reproducibility*
- *Linearity/Assay Reportable Range*
- *Detection limit*
- *Analytical Specificity*
- *Assay cut-off*
- *Method Comparison Studies*
- *Clinical Studies (Sensitivity, Specificity, and cut-off)*

9.2 Non-Clinical Performance Testing

9.2.1 *Stability Studies*

Stability studies were conducted to support the shelf life (unopened) and on-board (opened) material for the ADVIA Centaur VB12 MCMs to ensure that it maintains optimal product performance throughout the established shelf-life. The data supports the stability claims detailed in the ADVIA Centaur VB12 MCM Instructions for Use.

The following stability studies were performed for ADVIA Centaur VB12 MCM:

- Real Time/Shelf Life (unopened)
- On-Board

Real time shelf-life studies (unopened): Test VB12 MCMs were stored unopened at 2–8°C and tested at T=0 and at the following time points: 6 months, 12 months, and 15 months. Shelf life claims are based upon real time stability carried out one month after the duration claimed. Real time shelf-life stability studies of MCMs were determined by comparison of dose recoveries to the T=0 dose recovery results. Acceptance criteria for the real-time stability study were met up to the 15 months' time point, which supports a shelf-life claim of 14 months. Unopened storage shelf-life is indicated by the expiration date on the vial label.

On-board Stability: Pooled aliquots of test VB12 MCMs in sample cups were stored on the ADVIA Centaur system and measured at time point T= 0, 2, 4 and 5 hours. On-board stability studies of MCMs were determined by comparison of dose recoveries to the T=0 dose recovery results.Acceptance criteria for the on-board stability study were met up to 5 hours, which supports the on-board stability claim for 4 hours.

Stability Acceptance Criteria

The stability specifications acceptance criteria for the ADVIA Centaur VB12 MCM are as follows:

- Real Time/Shelf life (Unopened): The dose recovery for MCM1 must be ≤ 45 pg/mL dose; MCM2, the % dose recovery must be within 75 to 125%; MCM3–6, the % dose recovery must be within 85 to 115% calculated back to Day 0 and/or no adverse trends.
- On-Board: The dose recovery for MCM1 must be ≤ 45 pg/mL dose; MCM2, the % dose recovery must be within 75 to 125%; MCM3–6, the % dose recovery must be within 85 to 115% calculated to T=0.

9.2.2 *Value Assignment*

The ADVIA Centaur VB12 MCMs are value assigned using assigned reference calibrators and MCMs. The assigned reference calibrators are prepared using USP (United States Pharmacopeia) VB12 stock and are traceable to USP internal material. The MCMs are manufactured using qualified materials and measurement procedures.

For each new VB12 MCM lot manufactured, MCM1 is run in 5 replicates on two separate runs using one reagent kit lot. A nested testing run protocol is used for MCM2–MCM6 value assignment. This consists of running alternating samples of the reference and new MCM level in the same run. MCM2–MCM6 were tested on 20 replicates in total, comprised of one run and four sample cups run in 5 replicates on one system and one reagent kit lot. This protocol is designed to remove system and run variation. The new MCM doses must fall within the final value assignment specification for VB12 MCMs. The MCMs dose values are generated using the two-point calibration. The new MCM dose is calculated based on the relationship between the observed reference MCM dose and its assigned value. A performance verification run consisting of 6 replicates of each MCM level is run using one instrument, one reagent kit lot and Bio-Rad controls. The mean MCM doses of the new MCM lot manufactured must fall within the customer range specifications.

The target for MCM1 is assigned a 0.0 dose. The quality control specifications and final value assignment limits for VB12 MCM ensure that MCM1 measures at or below the VB12 assay sensitivity limit. MCM6 targeted greater than the assay range is diluted with the MCM1 to meet the reportable range of the assay.

9.2.3 *Expected Values*

The expected values are the lot-specific assigned values obtained at value assignment and the lot-specific assigned ranges are the lot-specific customer ranges are determined per % interval on page 6.

MCM Level	% Interval
MCM1	N/A
MCM2	50%
MCM3	25%
MCM4	25%
MCM5	25%
MCM6	20%

Lot-specific assigned values and ranges are provided in the ADVIA Centaur VB12 MCM lot-specific value sheet in the example provided in **Table 2.**

Table 2: *Example Lot-specific VB12 MCM Target and Assigned Values*

MCM Level	Target Values (pg/mL)	Assigned Values (pg/mL)
MCM1	0	0.00
MCM2	100	99.7
MCM3	250	218
MCM4	500	469
MCM5	1000	1099
MCM6	2200	2309
Assay Range	45–2000 pg/mL (33–1476 pmol/L)	

9.2.4 *Traceability*

The ADVIA Centaur VB12 assay is traceable to an internal standard manufactured using U.S.P. (United States Pharmacopeia) material. Assigned values for calibrators and MCMs are traceable to this standardization. The VB12 MCMs are manufactured using qualified materials and measurement procedures.

10. Proposed Labeling

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

11. Conclusion

The ADVIA Centaur VB12 Master Curve Material (MCM) is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the currently marketed Elecsys Vitamin B_{12} CalCheck. Based on the testing completed and the comparisons with predicate device, the ADVIA Centaur VB12 Maser Curve Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.

510(k) Summary – ADVIA Centaur ThCG Master Curve Material

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

The assigned 510(k) Number: k140505

1. Applicant Information	
Mailing Address:	Siemens Healthcare Diagnostics Inc. 511 Benedict Avenue Tarrytown, NY 10591 USA
Contact Person:	Fatima Pacheco Regulatory Clinical Affairs Specialist
Phone Number:	(914) 524-2450
Fax Number:	(914) 524-3579
E-mail Address:	fatima.pacheco@siemens.com
Date Prepared:	February 24, 2014
2. Device Name	**ADVIA Centaur® Total hCG Master Curve Material**
Proprietary Name:	Quality Control materials for ADVIA Centaur Total hCG assay
Measurand:	Master Curve Material (MCM) for ADVIA Centaur Total hCG
Type of Test:	assay
Regulation Section:	21 CFR 862.1660, Quality Control Material
Classification:	Class I Reserved
Products Code:	JJX – Single (Specified) Analyte Controls (Assayed and Unassayed)
Panel:	Clinical Chemistry (75)
3. Predicate Device Name	Elecsys HCG CalCheck 5
Predicate 510(k) No:	K092168
4. Device Description:	ADVIA Centaur® ThCG Master Curve Materials is an *in vitro* diagnostic product containing various levels of ThCG in lyophilized equine serum with preservatives including amphotericin B. Each set contains ten lyophilized levels (MCM1–10); with a reconstituted volume of 1.0 mL each. MCM1 contains no analyte. The ThCG MCMs assigned values are lot specific of target values: 0.0, 5.00, 10.0, 25.0, 50.0, 100, 250, 500, 750, and 1400 mIU/mL.
5. Intended Use:	See Indications for Use Statement below:
Indication for Use:	The ADVIA Centaur® Total hCG (ThCG) Master Curve Material is for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur ThCG assay.

Special Conditions for Use Statement(s): For prescription use only

Special Instrument Requirements: ADVIA Centaur® Systems
A description of the ADVIA Centaur system is documented in K971418. Subsequent modifications to the instrument have been reviewed and cleared in K032525 and K041133.

6. **Technological Characteristics and Substantial Equivalence Comparison with Predicate:** A comparison of the device features, intended use, and other information demonstrates that the ADVIA Centaur ThCG MCM is substantially equivalent to the predicate device as summarized in **Table 1**.

Table 1: Substantial Equivalence Comparison

SIMILARITIES		
	Candidate Device	**Predicate Device**
Item	ADVIA Centaur ThCG MCM	Elecsys HCG CalCheck 5
Intended Use	The ADVIA Centaur Total hCG (ThCG) MCM is for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur ThCG assay.	The Elecsys HCG CalCheck 5 is an assayed control for use in calibration verification and for use in the verification of the assay range established by the Elecsys HCG+β reagent and Elecsys HCG STAT reagent on the indicated Elecsys and cobas e immunoassay analyzers.
Analyte	HCG	Same
Use	Multiple Use	Same
Storage	2–8°C	Same
Form	Lyophilized	Same
DIFFERENCES		
Matrix	Equine Serum	Human Serum
Levels	10	5
Stability	**Unopened** – Stable when stored unopened at 2–8°C until the expiration date on the vial label. **Opened (Reconstituted)** – Stable when stored at 2–8°C for 28 days; or on-board for 4 hours.	**Unopened** – Stable at 2–8°C up to the expiration date printed on the bottle labels. **Opened (Reconstituted)** – Stable for 4 hours at 20–25°C.

7. Standard/Guidance Document References

The following recognized standard and guidance documents were used:

- CEN 13640 Stability Testing of In Vitro Diagnostic Reagents
- Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators
- Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material

8. **Test Principle**

The MCMs are specifically intended for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur assays for use on the ADVIA Centaur systems. Customers may use MCMs for bi-annual calibration verification checks of the assay range and linearity in order to meet the requirements of hospital accreditation bodies.

9. **Performance Characteristics**

9.1 Analytical performance:

The following studies are not applicable for the purpose of this submission:

- *Precision/Reproducibility*
- *Linearity/Assay Reportable Range*
- *Detection limit*
- *Analytical Specificity*
- *Assay cut-off*
- *Method Comparison Studies*
- *Clinical Studies (Sensitivity, Specificity, and cut-off)*

9.2 Non-Clinical Performance Testing

9.2.1 *Stability Studies*

Stability studies were conducted to support the shelf life unopened and reconstituted material for the ADVIA Centaur ThCG MCMs to ensure that it maintains optimal product performance throughout the established shelf-life. The data supports the stability claims detailed in the ADVIA Centaur ThCG MCM Instructions for Use.

The following stability studies were performed for ADVIA Centaur ThCG MCM:

- Real Time/Shelf Life (unopened)
- In Use Open Vial (Reconstituted)
- On-Board

Real time shelf-life studies (unopened): Test ThCG MCMs were stored unopened at 2–8°C and tested at T=0 and at the following time points: 6 months, 12 months, and 15 months. Shelf life claims are based upon real time stability carried out one month after the duration claimed. Real time shelf-life stability studies of MCMs were determined by comparison of dose recoveries to the T=0 dose recovery results. Acceptance criteria for the real-time stability study were met up to the 15 months' time point, which supports a shelf-life claim of 14 months. Unopened storage shelf-life is indicated by the expiration date on the vial label.

In-Use Open Vial (Reconstituted): Test ThCG MCMs were reconstituted, each level pooled, aliquotted and stored at 2–8°C, tested in 5 replicates per level at T=0, 7, 14, 21 28, and 29 days. Acceptance criteria for the open vial (reconstituted) stability study were met to the 29 days' time point, which supports the open vial claim of 28 days when properly stored at 2–8°C.

On-board Stability: Pooled aliquots of test ThCG MCMs in sample cups were stored on the ADVIA Centaur system and measured at time point T= 0, 2, 4 and 5 hours. Acceptance criteria for the on-board stability study were met up to 5 hours, which supports the on-board stability claim for 4 hours.

Stability Acceptance Criteria

The stability specifications acceptance criteria for the ADVIA Centaur ThCG MCM are as follows:

- Real Time/Shelf life (Unopened): The dose recovery for MCM1 must be ≤ 2.0 mIU/mL dose; MCM2–3, the % dose recovery must be within 80 to 120%; MCM4–10, the % dose recovery must be within 85 to 115% calculated to Day 0 and/or no adverse trends.
- In-Use Open Vial (Reconstituted): The dose recovery for MCM1 must be ≤ 2.0 mIU/mL dose; MCM2–3, versus -80°C MCM2–3 the average dose % dose recovery must be within 80 to 120%; MCM4–10, versus -80°C MCM4–10 the average dose % dose recovery must be within 85 to 115%.
- On-Board: The dose recovery for MCM1 must be ≤ 2.0 mIU/mL dose; MCM2–3, the % dose recovery must be within 80 to 120%; MCM4–10, the % dose recovery must be within 85% to 115% calculated to Time=0.

9.2.2 ***Value Assignment***

The ADVIA Centaur ThCG MCMs are value assigned using assigned reference calibrators and MCMs. The assigned reference calibrators are prepared using hCG stock and are traceable to internal material which is standardized against World Health Organization (WHO) 4th IS 75/589 reference material. The MCMs are manufactured using qualified materials and measurement procedures.

For each new ThCG MCM lot manufactured, MCM1 is run in 5 replicates on two separate runs using one reagent kit lot. A nested testing run protocol is used for MCM2–MCM10 value assignment. This consists of running alternating samples of the reference and new MCM level in the same run. MCM2–MCM10 were tested on 20 replicates in total, comprised of one run and four sample cups run in 5 replicates on one system and one reagent kit lot. This protocol is designed to remove system and run variation. The new MCM doses must fall within the final value assignment specification for ThCG MCMs. The MCMs dose values are generated using the two-point calibration. The new MCM dose is calculated based on the relationship between the observed reference MCM dose and its assigned value. A performance verification run consisting of 6 replicates of each MCM level is run using one instrument, one reagent kit lot and Bio-Rad controls. The

mean MCM doses of the new MCM lot manufactured must fall within the customer range specifications.

The target for MCM1 is assigned a 0.0 dose. The quality control specifications and final value assignment limits for ThCG MCM ensure that MCM1 measures at or below the ThCG assay sensitivity limit. MCM10 targeted greater than the assay range is diluted with the MCM1 to meet the reportable range of the assay.

9.2.3 *Expected Values*

The expected values are the lot-specific assigned values obtained at value assignment and the lot-specific assigned ranges are the lot-specific customer ranges are determined per % interval as below.

MCM Level	% Interval
MCM1	N/A
MCM2	35
MCM3	25
MCM4	25
MCM5	25
MCM6	25
MCM7	25
MCM8	25
MCM9	25
MCM10	25

Lot-specific assigned values and ranges are provided in the ADVIA Centaur ThCG MCM lot-specific value sheet in the example provided in **Table 2.**

Table 2: *Example Lot-specific ThCG MCM Target and Assigned Values*

MCM Level	Target Values (mIU/mL)	Assigned Values (mIU/mL)
MCM1	0.00	0
MCM2	5.00	4.39
MCM3	10.0	9.82
MCM4	25.0	21.5
MCM5	50.0	45.0
MCM6	100	94.3
MCM7	250	270
MCM8	500	557
MCM9	750	791
MCM10	1400	1393
Assay Range	2.0–1000 mIU/mL	

9.2.4 *Traceability*

The ADVIA Centaur ThCG assay is standardized against the WHO 4th IS 75/589 reference material. Assigned values for calibrators and MCMs are traceable to this standardization. The ThCG MCMs are manufactured using qualified materials and measurement procedures.

10. Proposed Labeling

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

11. Conclusion

The ADVIA Centaur ThCG Master Curve Material (MCM) is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the currently marketed Elecsys HCG CalCheck 5. Based on the testing completed and the comparisons with predicate device, the ADVIA Centaur ThCG Maser Curve Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.

510(k) Summary – ADVIA Centaur TSTO Master Curve Material

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

The assigned 510(k) Number: k140505

1. Applicant Information	
Mailing Address:	Siemens Healthcare Diagnostics Inc. 511 Benedict Avenue Tarrytown, NY 10591 USA
Contact Person:	Fatima Pacheco Regulatory Clinical Affairs Specialist
Phone Number:	(914) 524-2450
Fax Number:	(914) 524-3579
E-mail Address:	fatima.pacheco@siemens.com
Date Prepared:	February 24, 2014
2. Device Name	**ADVIA Centaur® Testosterone (TSTO) Master Curve Material**
Proprietary Name:	Quality Control materials for ADVIA Centaur TSTO assay
Measurand:	Master Curve Material (MCM) for ADVIA Centaur TSTO
Type of Test:	assay
Regulation Section:	21 CFR 862.1660, Quality Control Material
Classification:	Class I Reserved
Products Code:	JJX – Single (Specified) Analyte Controls (Assayed and Unassayed)
Panel:	Clinical Chemistry (75)
3. Predicate Device Name	Elecsys Testosterone CalCheck
Predicate 510(k) No:	K970146
4. Device Description:	ADVIA Centaur® TSTO Master Curve Materials is an *in vitro* diagnostic product containing various levels of testosterone spiked in lyophilized human plasma with sodium azide and preservatives. Each set contains seven lyophilized levels (MCM1–7); with a reconstituted volume of 1.0 mL each. MCM1 contains no analyte. The TSTO MCMs assigned values are lot specific of target values 0.00, 50.0, 100, 500, 750, 1000, and 1600 ng/dL. **CAUTION! POTENTIAL BIOHAZARD:** Contains human source material. While each human serum or plasma donor unit used in the manufacture of this product was tested by FDA-approved methods and found nonreactive for hepatitis B surface antigen (HBsAg), antibody to hepatitis C (HCV), and antibody

	to HIV-1/2, all products manufactured using human source material should be handled as potentially infectious. Because no test method can offer complete assurance that hepatitis B or C viruses, HIV, or other infectious agents are absent, these products should be handled according to established good laboratory practices.
5. **Intended Use:** **Indication for Use:**	See Indications for Use Statement below: The ADVIA Centaur® Testosterone (TSTO) Master Curve Material is for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur Testosterone assay.
Special Conditions for Use Statement(s):	For prescription use only
Special Instrument Requirements:	ADVIA Centaur® Systems A description of the ADVIA Centaur system is documented in K971418. Subsequent modifications to the instrument have been reviewed and cleared in K032525 and K041133.
6. **Technological Characteristics and Substantial Equivalence Comparison with Predicate:**	A comparison of the device features, intended use, and other information demonstrates that the ADVIA Centaur TSTO MCM is substantially equivalent to the predicate device as summarized in **Table 1**.

Table 1: Substantial Equivalence Comparison

SIMILARITIES		
	Candidate Device	**Predicate Device**
Item	ADVIA Centaur TSTO MCM	Elecsys Testosterone CalCheck
Intended Use	The ADVIA Centaur Testosterone (TSTO) MCM is for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur TSTO assay.	For use in the verification of the calibration established by the Elecsys Testosterone reagent on the indicated Elecsys and cobas e immunoassay analyzers.
Analyte	Testosterone	Same
Use	Multiple Use	Same
Storage	2–8°C	Same
Form	Lyophilized	Same
DIFFERENCES		
Matrix	Human Plasma	Human Serum
Levels	7	3
Stability	**Unopened** – Stable when stored unopened at 2–8°C until the expiration date on the vial label. **Opened (Reconstituted)** – Stable when stored at 2–8°C for 14 days; or on-board for 4 hours.	**Unopened** – Stable at 2–8°C up to the expiration date printed on the bottle labels. **Opened (Reconstituted)** – Stable for 4 hours at 15–25°C.

7. Standard/Guidance Document References

The following recognized standard and guidance documents were used:

- CEN 13640 Stability Testing of In Vitro Diagnostic Reagents
- Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators
- Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material

8. Test Principle

The MCMs are specifically intended for *in vitro* diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur assays for use on the ADVIA Centaur systems. Customers may use MCMs for bi-annual calibration verification checks of the assay range and linearity in order to meet the requirements of hospital accreditation bodies.

9. Performance Characteristics

9.1 Analytical performance:

The following studies are not applicable for the purpose of this submission:

- *Precision/Reproducibility*
- *Linearity/Assay Reportable Range*
- *Detection limit*
- *Analytical Specificity*
- *Assay cut-off*
- *Method Comparison Studies*
- *Clinical Studies (Sensitivity, Specificity, and cut-off)*

9.2 Non-Clinical Performance Testing

9.2.1 *Stability Studies*

Stability studies were conducted to support the shelf life unopened and reconstituted material for the ADVIA Centaur TSTO MCMs to ensure that it maintains optimal product performance throughout the established shelf-life. The data supports the stability claims detailed in the ADVIA Centaur TSTO MCM Instructions for Use.

The following stability studies were performed for ADVIA Centaur TSTO MCM:

- Real Time/Shelf Life (unopened)
- In Use Open Vial (reconstituted)
- On-Board

Real time shelf-life studies (unopened): Test TSTO MCMs were stored unopened at 2–8°C and tested at T=0 and at the following time points: 12 months, 18 months, and 21 months. Shelf life claims are based upon real time stability carried out one month after the duration claimed. Real time shelf-life stability studies of MCMs were determined by comparison of dose recoveries to the T=0 dose recovery results. Acceptance criteria for the real-time stability study were met up to the 21 months' time point, which supports a shelf-life claim of 20 months. Unopened storage shelf-life is indicated by expiration date on the vial label.

In use open vial (reconstituted) stored at 2–8°C: Test TSTO MCMs were reconstituted, each level pooled, aliquotted and stored at 2–8°C, tested in 5 replicates per level at T=0, 2, 4, 7, 8, 11, 14 and 15 days. Acceptance criteria for the open vial (reconstituted) stability study were met up to the 15 day time point, which supports the open vial claim of 14 days when stored at 2–8°C.

On-board Stability: Pooled aliquots of test TSTO MCMs in sample cups were stored on the ADVIA Centaur system and measured at time point T= 0, 2, 4 and 5 hours. Acceptance criteria for the on-board stability study were met up to 5 hours, which supports the on-board stability claim for 4 hours.

Stability Acceptance Criteria

The stability specifications acceptance criteria for the ADVIA Centaur TSTO MCM are as follows:

- Real Time/Shelf life (Unopened): The dose recovery for MCM1 must be ≤ 10.0 ng/dL dose; MCM2–3, the average % dose recovery must be within 75 to 125%; MCM4–7, the average % dose recovery must be within 85 to 115% calculated to Day 0 and/or no adverse trends.

- In Use Open Vial (reconstituted): The dose recovery for MCM1 versus freshly reconstituted -80°C stored MCM1 average dose must be ≤ 10.0 ng/dL dose; for MCM2–3 versus freshly reconstituted -80°C stored MCM2–3 average dose, the average % dose recovery must be within 75 to 125%; MCM4–7 versus freshly reconstituted -80°C stored MCM4–7 average dose, the average % dose recovery must be within 85 to 115%.

- On-Board: The dose recovery for MCM1 must be ≤ 10.0 ng/dL dose; MCM2–3, the % dose recovery must be within 75 to 125%; MCM4–7, the % dose recovery must be within 85 to 115% calculated to Time=0.

9.2.2 *Value Assignment*

The ADVIA Centaur TSTO MCMs are value assigned using assigned reference calibrators and MCMs. The assigned reference calibrators are prepared using USP (United States Pharmacopeia) testosterone stock and are traceable to analytically prepared internal material which are traceable to gas-chromatography-mass spectroscopy (GCMS). The MCMs are manufactured using qualified materials and measurement procedures.

For each new TSTO MCM lot manufactured, MCM1 is run in 5 replicates on two separate runs using one reagent kit lot. A nested testing run protocol is used for MCM2–MCM7 value assignment. This consists of running alternating samples of the reference and new MCM level in the same run. MCM2–MCM7 were tested on 20 replicates in total, comprised of one run and four sample cups run in 5 replicates on one system and one reagent kit lot. This protocol is designed to remove system and run variation. The new MCM doses must fall within the final value assignment specification for TSTO MCMs. The MCMs dose values are generated using the two-point calibration. The new MCM dose is calculated based on the relationship between the observed reference MCM dose and its assigned value. A performance verification run consisting of 6 replicates of each MCM level is run using one instrument, one reagent kit lot and Bio-Rad controls. The mean MCM doses of the new MCM lot manufactured must fall within the customer range specifications.

The target for MCM1 is assigned a 0.0 dose. The quality control specifications and final value assignment limits for TSTO MCM ensure that MCM1 measures at or below the TSTO assay sensitivity limit. MCM7 targeted greater than the assay range is diluted with the MCM1 to meet the reportable range of the assay.

9.2.3 *Expected Values*

The expected values are the lot-specific assigned values obtained at value assignment and the lot-specific assigned ranges are the lot-specific customer ranges as determined per % interval as below.

MCM Level	% Interval
MCM1	N/A
MCM2	25
MCM3	25
MCM4	25
MCM5	25
MCM6	25
MCM7	20

Lot-specific assigned values and ranges are provided in the ADVIA Centaur TSTO MCM lot-specific value sheet in the example provided in **Table 2.**

Table 2: *Example Lot-specific TSTO MCM Target and Assigned Values*

MCM Level	Target Values (ng/dL)	Assigned Values (ng/dL)
MCM1	0	0.00
MCM2	50.0	65.2
MCM3	100	109
MCM4	500	557
MCM5	750	807
MCM6	1000	1004
MCM7	1600	1575
Assay Range	10–1500 ng/dL (0.35–52.1 nmol/L)	

9.2.4 *Traceability*

The ADVIA Centaur TSTO assay is traceable to an internal standard manufactured analytically which is traceable to gas chromatography-mass spectroscopy (GC-MS). The following equation describes the relationship between the testosterone standards and GCMS analysis throughout the assay range.

ADVIA Centaur Testosterone = 1.00 (GCMS) + 1.35 ng/dL, r = 1.00

Assigned values for calibrators and MCMs are traceable to this standardization. The TSTO MCMs are manufactured using qualified materials and measurement procedures.

10. Proposed Labeling

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

11. Conclusion

The ADVIA Centaur TSTO Master Curve Material (MCM) is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the currently marketed Elecsys Testosterone CalCheck. Based on the testing completed and the comparisons with predicate device, the ADVIA Centaur TSTO Maser Curve Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

March 31, 2014

SIEMENS HEALTHCARE DIAGNOSTICS INC.
FATIMA PACHECO
511 BENEDICT AVENUE
TARRYTOWN NY 10591-5097

Re: K140505
Trade/Device Name: ADVIA Centaur® Vitamin B12 (VB12) Master Curve Material
ADVIA Centaur® Total Hcg (ThCG) Master Curve Material
ADVIA Centaur® Testosterone (TSTO) Master Curve Material
Regulation Number: 21 CFR 862.1660
Regulation Name: Quality control material (assayed and unassayed)
Regulatory Class: I, Reserved
Product Code: JJX
Dated: February 24, 2014
Received: February 27, 2014

Dear Ms. Pacheco:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement on last page.

510(k) Number *(if known)*
k140505

Device Name
ADVIA Centaur Vitamin B12 Master Curve Material, Total hCG Master Curve Material, and Testosterone Master Curve Material

Indications for Use *(Describe)*
The ADVIA Centaur® Vitamin B12 (VB12) Master Curve Material is for in vitro diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur VB12 assay.

The ADVIA Centaur® Total hCG (ThCG) Master Curve Material is for in vitro diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur ThCG assay.

The ADVIA Centaur® Testosterone (TSTO) Master Curve Material is for in vitro diagnostic use in the verification of calibration and reportable range of the ADVIA Centaur Testosterone assay.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Yung W. Chan -S

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